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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/786,988	01/23/1997	DANIEL P. LITTLE	24736-2001D	5922

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EXAMINER	
GAKH, YELENA G	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 07/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/786,988	LITTLE ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *108-134,139,140 and 144-146* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *108-134,139,140 and 144-146* is/are rejected.

7)☒ Claim(s) *119* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. As a result of the Pre-Appeal Conference held on 06/08/06 the examiner withdraws the finality of the last Office action and reopens the case.

Examiner's Amendment

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Bruce D. Grant on 07/17/06.

The application has been amended as follows:

Cancel claims 135-138 and 141-143.

As a result of the amendment claims 108-134, 139-140 and 144-146 are pending in the application.

Claim Objections

3. Claim 119 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 119 recites 3-hydroxypicolinic acid, which is already recited in parent claim 108.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 144 and 145 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Since it may be assumed that the spots formed on the substrate are circular, it is not clear, which two dimensions 450μm x 450μm or 800μm x 800μm are meant in defining the spot size. Moreover, the area of the spot would not be calculated as 450 x 450 μm^2, if 450μm is the spot diameter (D). It rather will be less than this product ($\pi/4D^2$).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the

examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. **Claims 108-134, 139-140 and 144-146** are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. (US 5,658,802, IDS) in view of Hancock et al. (US 5,716,825, IDS) and Zhang et al. (JMS Letters).

Hayes teaches "method and apparatus for making miniaturized diagnostic arrays" using electro-mechanical or piezoelectrical dispensers to place extremely small drops (10 pl to 1 nl) of fluid on substrates to form diagnostic arrays. Hayes indicates, "the invention thus provides a highly accurate, rapid and repeatable method of placing extremely small drops (10 pl to 1 nl) of fluid reagent on substrates to form diagnostic arrays. By using such small drops and accurately positioning them on the substrate, test strips can be formed which have a larger number of probes located within a smaller area than is achievable with prior methods" (col. 2, lines 49-55). Hayes method utilizing piezoelectrical dispensers covers all limitations of the claims directed toward depositing by piezoelectric dispenser (claims 108-118, 134, 139-140, 144-145).

Hayes does not specifically disclose depositing 3-hydroxypicolinic acid on various MALDI substrates recited in the claims.

Hancock discloses an integrated nucleic acid analysis system for MALDI-TOF MS, and describes in particular a thin film sample support, which is a substantially "planar manifold made of a non-conducting material that includes a microchannel and other necessary components of a miniturized sample preparation compartment, an interface to non-consumable parts, and an ionization surface for MALDI-TOF MS. Such a miniaturized device may be formed from a variety of materials (e. g., **silicon, glass, low cost polymers**) by techniques that are well known in the art (e.g., micromachining, chemical etching, laser ablation, and the like)" (col. 4,11. 34-44). Hancock further describes a process wherein analyte is embedded in a solid or crystalline "matrix" of light-absorbing molecules (e. g., **nicotinic, sinapinic, or 3-hydroxypicolinic acid**) (col. 6,11. 15-25). Hydrophobic and hydrophilic MALDI ionization surfaces, such as metals (**gold, copper, stainless steel**), glass, silica, nylon and other synthetic polymers, agarose and other carbohydrate polymers, and plastics are disclosed as surfaces for actively capturing analyte (col. 6,11. 38-44). Other capture regions are disclosed, such as **surface of a bead, particle** or planar support treated with a bifunctional cross-linking reagent. "According to the practice of the present invention, a capture region may be formed in any microstructure surface in the sample

preparation compartment by linking an analyte binding partner directly to the surface, and on MALDI ionization surfaces integrated with the preparation compartment. Alternatively, a capture region may be formed on the surfaces of beads, which can be chemically attached to the surface of the support, or magnetically attached by using magnetically responsive beads and applying a magnetic field to anchor the beads to the desired region of the support. Magnetically responsive beads and particles are well-known in the art and are commercially available from, for example, Dynal. RTM., Inc. (Lake Success, N.Y.) and Bangs Laboratories, Inc. (Carmel, Ind.)" (col. 7, 11. 30-43).

Hancock does not specifically teach depositing 0.2-20 nL of the matrix on the substrate.

Zhang teaches a method and an apparatus for dispensing a target material on a multi-well sample holder (substrate) (Fig. 1, page 1769, line 6-8). The method comprises the steps of providing a packed capillary (i.e. vesicle) having an interior chamber containing a fluid, disposing the vesicle adjacent a first location on the surface of the substrate and ejecting a defined and controlled ~5 nL volume of the fluid, while evaporating the solvent forms a spot of the sample of less than 0.3 mm^2. MALDI-MS analysis is performed directly from the spot. The chamber is rinsed with a washing solution (Figure 1, page 1768, right column). It is absolutely clear from Figure 1 and its caption that the vesicle is moved from spot to spot to repeat these steps for each location (each well) of the multi-well holder, with ~ 5 nL of the sample fraction deposited in each spot. The accuracy of the volume is given exactly with the same precision as the one disclosed in the specification of the instant application: "into each well was dispensed 20 droplets (~ 5 nL) of 3-HPA matrix solution" (page 26, the last paragraph).

Since it is notoriously well known in the art of mass spectrometry that quality of MALDI spectra strongly depends on quality of matrix crystals, it would have been obvious for any person of ordinary sill in the art to deposit exact amount of 3-hydroxypicolinic acid, which is used as a MALDI matrix for nucleic acids as taught by Hancock using Handy's technique of accurate depositing reagents on the substrate and evaporate the solvent in order to perform high throughput X-ray or microscopic analysis of 3-hydroxypicolinic acid crystals formed on MALDI substrate for the volumes indicated by Zhang.

Response to Arguments

9. Applicant's arguments filed 05/01/06 have been fully considered but they are moot in light of new grounds for rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

7/17/06

YELENA GAKH
PRIMARY EXAMINER